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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,101	BOTT ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/31/05, 1/13/05, 2/25/04, 12/5/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The reply received 11/28/05 canceling claims 1-55 and amending claims 68-71 is acknowledged. Claims 56-71 are pending.

Election/Restrictions

Applicant's election without traverse of Group III, claims 56-67, in the reply filed on 11/28/05 is acknowledged. Applicant's election without traverse of various species in the same reply is acknowledged. The restriction is made FINAL. New claims 68-71, which are drawn to the elected species, have been added to the elected Group. Examination will commence at this point on claims 56-71 ONLY.

Claim Objections

Claim 67 is objected to because of the following informalities: The word "that" seems to have been omitted from line 6, after the word "such." Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 57, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for removing necrotic tissue in the immediate vicinity of the skin to which the topical preparation has been applied, does not reasonably provide enablement for removing any necrotic tissue from any source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The claims have been interpreted (see below rejections under 35 U.S.C. § 112, second paragraph) as being broadly drawn to a method comprising placing a topical preparation (which comprises an active agent; see rejection of claim 56 under 35 U.S.C. § 112, second paragraph, below) in contact with the skin of a patient, such that the active agent is released onto said skin, thus removing necrotic tissues. In claim 66, the composition causes "necrotic tissues covered by said topical preparation," and the active agent selectively removes the resulting swollen necrotic tissues.

The breadth of the limitation "necrotic tissues" is not supported by the specification. Claims 57 and 67 do not require that the necrotic tissues have any structural, functional, or proximal relationship to the site of contact. The claims read, therefore, on applying a topical composition comprising collagen (a structural protein) as an active agent to the upper arm, thereby removing necrotic tissue from the liver. The claims even read on applying a topical composition comprising sucrose (a food source) as an active agent to the upper arm of a patient, thereby removing necrotic tissue from

the liver of the patient's mother. The limitation "necrotic tissues covered by said topical preparation" does not fully rectify the problem, because it reads on applying a topical composition comprising glucokinase (an enzyme involved in glucose metabolism) as an active agent to the upper arm, thereby removing necrotic tissue from the humerus (which is covered by muscle, which is covered by the skin of the upper arm, which is covered by the topical composition).

In addition to the fact that the claims currently read on removing any necrotic tissue from any location by the claimed application method, the claims are problematic in that the person of ordinary skill in the art would not have a reasonable expectation that any given active agent would remove necrotic tissue even if applied directly thereto. Even if "active agent" is interpreted as "enzyme" (which the examiner does not concede; see below rejections under section 112, second paragraph), the person of ordinary skill in the art would not have a reasonable expectation that any given enzyme would have the desired outcome, *i.e.* removal of necrotic tissue. For example, glucokinase is certainly an enzyme, but the skilled artisan would have no reason to expect that glucokinase would have any activity in removing necrotic tissue from any site, since it is a metabolic enzyme.

The specification and prior art provide insufficient evidence that the person of ordinary skill in the art would have a reasonable expectation of success in removing all necrotic tissues by the topical application of any topical composition (comprising any given active agent, regardless of the definition thereof) fulfilling the limitations of claim 56. The specification presents a narrow working embodiment in which eschar

(sloughed-off dead tissue from a wound) is soaked in a few solutions of proteases (protease B subtilisin, *C. histolyticum* collagenase, and protease from *B. subtilis* LG12; Examples 11-14). At no point is a composition in accordance with the claims applied to skin and necrotic tissue shown to be removed. Indeed, the results of the eschar-soaking experiments do not explicitly show that any tissue is degraded: "The [eschar samples treated with collagenase] had a lower percent weight gain **presumably due to** degradation of the eschar. The protease samples also had a lower percent weight gain **presumably due to** degradation of the eschar" (page 38, lines 20-22). There is no substantive evidence that eschar is "removed," or that it becomes "swollen" as a result of contact with the enzymes, as the claims require.

While a narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the direction applicants present, provides additional weight to the lack of enablement in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

Claims 59-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988); these factors can be found above.

The cited claims have been interpreted (see below rejections under 35 U.S.C. § 112, second paragraph) as being broadly drawn to a method comprising placing a topical preparation (which comprises an active agent; see rejection of claim 56 under 35 U.S.C. § 112, second paragraph, below) in contact with the skin of a patient, such that the active agent is released onto said skin, thus sterilizing a wound on the skin, preventing infection of the skin, and accelerating healing of a wound on the skin, respectively, for purposes of this rejection only.

As discussed above, the claims are problematic in that the person of ordinary skill in the art would not have a reasonable expectation that any given active agent would sterilize a wound, prevent infection, and/or accelerate wound healing, even if applied directly to the affected skin. Even if "active agent" is interpreted as "enzyme" (which the examiner does not concede; see below rejections under section 112, second paragraph), the person of ordinary skill in the art would not have a reasonable expectation that any given enzyme would have any of the outcomes recited in claims 59-61. For example, glucokinase is certainly an enzyme, but the skilled artisan would have no reason to expect that glucokinase would sterilize a wound, prevent infection, and/or accelerate wound healing, since it is a metabolic enzyme.

Furthermore, as discussed above, the working embodiment is narrow and does not address all of the outcomes in claims 59-61. As discussed above, the specification

presents a narrow working embodiment in which eschar is soaked in a few solutions of proteases (Examples 11-14). At no point is a composition in accordance with the claims applied to skin and a wound being sterilized thereby; anti-infection properties imparted thereby; or wound healing accelerated thereby. In fact, the specification does not address these requirements at all, much less provide sufficient guidance to use the claimed method for the outcomes of claims 59-61. The specification provides no guidance for selecting an enzyme that would sterilize a wound, provide anti-infection properties, and/or accelerate wound healing. In short, the specification as filed is insufficient to support these claims.

While a narrow working embodiment cannot be a sole factor in determining enablement, its limited showing, in light of the unpredictable nature of the art and the direction applicants present, provides additional weight to the lack of enablement in consideration of the *Wands* factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

Claims 57-61, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

M.P.E.P. § 2163 recites, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such

descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention... one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

In this case, the claims are broadly drawn to compositions comprising various active agents (see rejection of claim 56 under 35 U.S.C. § 112, second paragraph, below) that may have various effects. In the interest of compact prosecution, agents that "may have" a given property have been interpreted as agents that *have* the property (see rejection of claims 57-61 and 66 under 35 U.S.C. § 112, second paragraph, below) for this rejection only. Claim 67 also recites a second active agent that inhibits the first active agent. The specification, however, provides no criteria by which active agents that have the properties in claims 57-61 and 66 might be selected without extensive experimentation, even if "active agent" is interpreted as meaning "protein" or "enzyme" (which the examiner does not concede). Likewise, no criteria are provided for selecting an effective inhibitor for a given active agent, even if "active agent" is interpreted as meaning "protein" or "enzyme" (which the examiner does not concede).

M.P.E.P. §2163 recites, "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between

function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus...when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. **For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.**"

The specification allows that the active agents of the invention "are generally proteins, such as enzymes...enzymes suitable for [use in the invention] may be any enzyme or enzymes" and continues to imply that virtually any enzyme, from any source, having any activity, is contemplated by the invention (specification, page 12, line 7, through page 15, line 14). At no point, however, does the applicant provide any evidence toward a reasonable expectation that a given enzyme from pages 12-15 would have any of the activities recited in claims 57-61 and 66 or any guidance for choosing an enzyme from this list that has the desired activity. As discussed above, applicant's examples show that a few proteases have some effect on eschar *in vitro* (protease B subtilisin, *C. histolyticum* collagenase, and protease from *B. subtilis* LG12; Examples 11-14). At no point are the activities of claims 57-61 and 66 correlated with the enzymes listed at pages 12-15. The person of ordinary skill in the art would not immediately envisage the structures and sequences of the enzymes having the claimed properties from the information provided and the knowledge in the prior art.

Likewise, claim 67 recites the inclusion of "at least one second active agent selected such [that] said second active agent inhibits said [first] active agent," but the

specification provides no guidance for identifying an inhibitor for every enzyme listed at pages 12-15. At page 19, line 21, through page 20, line 7, the specification suggests the inclusion of a second active agent and provides a few examples for potential inhibitors of a few proteases, but no guidance is provided for the selection of an inhibitor of, for example, any given pectinase (one of the enzymes contemplated for use in the invention; page 12, line 13). The specification does not provide any criteria that link the function of said inhibitor with a given structure or sequence.

For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length. Although structural formulas provide a convenient method of demonstrating possession of specific molecules, other identifying characteristics or combinations of characteristics may demonstrate the requisite possession. Written description" requirement may be satisfied by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that **fully set forth** the claimed invention. See *Noelle v. Lederman*, 355 F.3d 1343, 1349, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) and *Lockwood v. American Airlines, Inc.*, 107 F.3d at 1572, 41 USPQ2d at 1966. A definition by function alone "does not suffice" to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Regents of the University of California v. Eli Lilly & Co.,* 119 F.3 at 1568, 43 USPQ2d at 1406 (Fed. Cir. 1997). See also *Fiers v. Ravel*, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (Fed. Clarification is required. 1993) (discussing *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991)). See M.P.E.P. § 2163.

In this case, the active agents and inhibitors are claimed and described only by their activities, not by structural or sequence limitations that would correlate a given active agent to a given activity and a given inhibitor to a given active agent. As such, the requirement for written description of biomolecules has not been fulfilled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 56-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 56 recites "an active agent," which has multiple meanings in the art. Consistent with the well-established axiom in patent law that a patentee or applicant is free to be his or her own lexicographer, a patentee or applicant may use terms in a manner contrary to or inconsistent with one or more of their ordinary meanings if the written description clearly redefines the terms. See, e.g., *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). Accordingly, when there is more than one definition for a term, **it is incumbent upon applicant to make clear which definition is being relied upon to claim the invention.** Until the meaning of a term or phrase used in a claim is clear, a rejection under 35 U.S.C. 112, second paragraph is appropriate. See *Tex. Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1202, 64 USPQ2d 1812, 1818 (Fed. Cir. 2002). See M.P.E.P. § 2173.05(a). It is noted that at page 6, lines 1-2, the specification recites:

> *Active Agent* shall be understood as referring to proteins, and in particular to enzymes.

This definition, however, does not meet the standard for a clear definition of a claim term, because the specification also recites:

- The active agents may perform a variety of functions. For example, the matrix can release proteases **and other enzymatic debriding agents** topically...clotting formation and clot removal enzymes, agents which generate...activated oxygen species, and anti-adhesion catalytic antagonists...and agents for skin treatment **and the like** (page 15, lines 9-14; emphasis added).
- [Regarding the second active agent, as recited in claim 67:] The adhesive may comprise...an active agent that is selected to inhibit the [first] active agent selected to remove necrotic tissue so that the healthy tissue is protected...For example, if the [first] active agent in the preparation over the wound comprises a protease, the [second] active agent in the adhesive may be a protease inhibitor. Examples of protease inhibitors include, **but are not limited to,** serine protease inhibitors such as those found in the serpin, Kunitz, Kazal, and leukoproteinase classes of inhibitors (page 19, line 19, through page 20, line 5; emphasis added).

The definition of the term "active agent" is not clearly pointed out within the specification, since, for example, the exemplary protease inhibitors at page 20, lines 4-5, are not enzymes, and not all protease inhibitors are proteins.

The specification does not explicitly equate the term "active agent" with "protein" or "enzyme," but rather states that the term refers in some way to proteins. It is not clear whether applicant means to claim only proteins, particularly enzymes, in claim 56, or whether any agent that is related in some manner to proteins would fulfill the requirement of the limitation. If the former is the case, applicant is urged to replace "active agent" with "protein" or "enzyme" in the claims wherever it appears, such that this source of confusion is allayed. Clarification is required. In the interest of compact

prosecution, the term "active agent" has been afforded its plain meaning, *i.e.*, any agent with an activity.

Because claims 57-67 depend from indefinite claim 56 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claims 57-61 are confusing because they allow that the active agent "may" have various properties; these limitations do not describe properties exhibited in the claimed composition, and they do not even require that the active agent possess these properties. A recitation of "preferred" conditions does not precisely define the metes and bounds of the claims. It is not clear whether any conditions other than the recited conditions are part of the claimed invention. Clarification is required.

Claim 57 recites the limitation "necrotic tissues" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 56 does not recite or imply any necrotic tissues, so it is not clear how the necrotic tissues of claim 57 are related to the skin or to the claimed topical preparation. Clarification is required.

Claim 59 allows that the "active agent may self-sterilize a wound." The term "self-sterilize" implies that the active agent sterilizes itself, or that the wound sterilizes itself, but the active agent may not sterilize the wound if this phrase is employed. Clarification is required. In the interest of compact prosecution, this limitation has been interpreted as "active agent may sterilize a wound."

Claim 60 allows that the active agent provide anti-infection properties, but it is not clear whether this "providing" is an active method step or the result of an inherent property of the active agent. Clarification is required.

Claim 61 allows that the active agent accelerate healing of a wound, but no point of reference is provided for the relative term "accelerate." No criteria are provided for assessing the speed of healing, and no limits are placed on the degrees of acceleration that are encompassed and excluded by the claim. Clarification is required.

Claims 62-65 are incomplete in that they omit essential elements, such omission amounting to a gap between the elements. See M.P.E.P. § 2172.01. The omitted elements in claims 62-65 are: A correlation between cross-link density and rate of active agent release from the composition; a correlation between choice of hydrophilic component and rate of active agent release from the composition; a correlation between patch thickness and rate of active agent release from the composition; and a correlation between occlusivity to air and rate of active agent release from the composition, respectively. The claims should be amended to particularly point out the manner in which these properties relate to rate of active agent release from the composition, and the criteria used to select the cross-link density, hydrophilic component, patch thickness, and occlusivity to air such that the desired rate is achieved.

Claim 62 is further confusing in that it requires that the cross-link density be "suitable for" providing a desired rate of active agent release, but not necessarily that said density actually provide said desired rate. Clarification is required. In the interest of compact prosecution, "a cross-link density suitable for providing a desired rate" has been interpreted as "a cross-link density that provides a desired rate."

Claim 62 recites the limitation "a cross-link density" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 56 does not recite any crosslinking. Clarification is required.

Claim 66 is confusing because it allows that the active agent "may" remove necrotic tissues; this limitation does not describe properties exhibited in the claimed composition, and it does not even require that the active agent possess this property. A recitation of "preferred" conditions does not precisely define the metes and bounds of the claims. It is not clear whether any conditions other than the recited conditions are part of the claimed invention. Clarification is required.

Claim 66 allows that the "active agent may remove necrotic tissues upon release from [the] silicone matrix," which is confusing because it is not clear whether the active agent, the necrotic tissues, or both are released from the matrix. Clarification is required. In the interest of compact prosecution, the first possibility is assumed to be the case.

Claim 66 requires that the occlusivity to fluid promote a moist environment that allows swelling of necrotic tissues, but it is not clear whether these "promoting" and "allowing" elements require active method steps, or whether they are inherent properties correlated with a particular occlusivity. Clarification is required.

Claims 66 and 67 recite the limitation "necrotic tissues" in various lines. There is insufficient antecedent basis for this limitation in the claim. Claim 56 does not recite or imply any necrotic tissues, so it is not clear how the necrotic tissues of claims 66 and 67 are related to the skin or to the claimed topical preparation. Clarification is required.

Claim 67 is incomplete in that it omits essential elements, such omission amounting to a gap between the elements. See M.P.E.P. § 2172.01. The omitted element is: A correlation between choice of second active agent and inhibition of the first active agent. The claims should be amended to particularly point out the manner in which these properties are related, and the criteria used to select the second active agent such that the desired inhibition is achieved.

Claim 67 requires that the second topical preparation be placed "around" a wound on the skin; it is not clear whether this limitation means "in the vicinity of" or "surrounding." Clarification is required. In the interest of compact prosecution, and in light of the limitations at lines 13-14, the latter is assumed to be the case.

Claim 67 recites "said topical preparation" at line 13, which is confusing because the claim refers to two different topical preparations. It is not clear which preparation is referenced by this limitation. Clarification is required. In the interest of compact prosecution, "said topical preparation" at line 13 has been interpreted as "the topical preparation of claim 56."

Regarding the recitation of "second active agent" in claim 67, see the above rejection of claim 56 under 35 U.S.C. § 112, second paragraph.

Claim 71 is confusing because it recites an abbreviation or symbol, LG12, without particularly defining the same within the claim. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 56-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Pfister et al. (1993, U.S. Patent 5,232,702; reference A). The claims are drawn to a method of providing an active agent topically comprising providing a topical preparation comprising an internal phase and an external phase, wherein the internal phase is dispersed within the external phase; the internal phase comprises at least one hydrophilic carrier and at least one active agent; and the external phase comprises a silicone matrix; and placing said preparation in contact with the skin of a patient such that said active agent is released from said matrix topically onto said skin. In some dependent claims, the active agent may have particular activities. In some dependent claims, the topical preparation has certain physical properties.

Pfister et al. teach silicone emulsions comprising a silicone phase and an organic phase, wherein the silicone phase comprises a cross-linked silicone elastomer and the organic phase is dispersed within the silicone phase (column 2, lines 5-30). Pfister et al. also teach applying the emulsions to the skin (Example D).

Claims 57-61 recite optional properties of the active agent; they do not require that the active agent possess the recited properties. As such, Pfister et al. reads on those embodiments for which the active agents do not necessarily have the properties recited in claims 57-61.

Claims 62-65 recite various physical properties of the topical composition. The composition of Pfister et al. comprises cross-linked silicone (column 4, lines 59-60), so it

has an inherent cross-link density. The composition comprises a hydrophilic component (column 2, lines 5-30). The composition is a topical patch, so it has an inherent thickness. The composition has an occlusivity to air, which may be zero or greater than zero. In any case, the active agent of Powell et al. is released at some rate, and the compositions inherently possess the physical properties of claims 62-65.

Claims 56-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Powell et al. (2000, U.S. Patent 6,060,546; reference B). The claims are drawn to a method of providing an active agent topically comprising providing a topical preparation comprising an internal phase and an external phase, wherein the internal phase is dispersed within the external phase; the internal phase comprises at least one hydrophilic carrier and at least one active agent; and the external phase comprises a silicone matrix; and placing said preparation in contact with the skin of a patient such that said active agent is released from said matrix topically onto said skin. In some dependent claims, the active agent may have particular activities. In some dependent claims, the topical preparation has certain physical properties.

Powell et al. teach silicone emulsions comprising a silicone phase and an organic phase, wherein the silicone phase comprises a cross-linked silicone elastomer and the organic phase is dispersed within the silicone phase (Abstract; column 3, lines 13-16). Powell et al. also teach applying the emulsions to the skin (Example 12).

Claims 57-61 recite optional properties of the active agent; they do not require that the active agent possess the recited properties. As such, Powell et al. reads on

those embodiments for which the active agents do not necessarily have the properties recited in claims 57-61.

Claims 62-65 recite various physical properties of the topical composition. The composition of Powell et al. comprises cross-linked silicone (see Example 3), so it has an inherent cross-link density. The composition comprises a hydrophilic component (column 3, lines 13-16). The composition is a topical patch, so it has an inherent thickness. The composition has an occlusivity to air, which may be zero or greater than zero. In any case, the active agent of Powell et al. is released at some rate, and the compositions inherently possess the physical properties of claims 62-65.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 56-65 and 68-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Pfister et al. (reference A) or Powell et al. (reference B). The

claims are drawn to a method of providing an active agent topically comprising providing a topical preparation comprising an internal phase and an external phase, wherein the internal phase is dispersed within the external phase; the internal phase comprises at least one hydrophilic carrier and at least one active agent; and the external phase comprises a silicone matrix; and placing said preparation in contact with the skin of a patient such that said active agent is released from said matrix topically onto said skin. In some dependent claims, the active agent may have particular activities. In some dependent claims, the topical preparation has certain physical properties. In some dependent claims, the hydrophilic carrier is polypropylene glycol. In some dependent claims, the enzyme is a hydrolase, specifically a protease, specifically LG12.

As discussed above, Pfister et al. teach silicone emulsions comprising a silicone phase and an organic phase, wherein the silicone phase comprises a cross-linked silicone elastomer and the organic phase is dispersed within the silicone phase (column 2, lines 5-30). Pfister et al. also teach applying the emulsions to the skin (Example D).

As discussed above, Powell et al. teach silicone emulsions comprising a silicone phase and an organic phase, wherein the silicone phase comprises a cross-linked silicone elastomer and the organic phase is dispersed within the silicone phase (Abstract; column 3, lines 13-16). Powell et al. also teach applying the emulsions to the skin (Example 12).

Claims 57-61 recite optional properties of the active agent; they do not require that the active agent possess the recited properties. As such, Pfister et al. and Powell et

al. read on those embodiments for which the active agents do not necessarily have the properties recited in claims 57-61.

Claims 62-65 recite various physical properties of the topical composition. The compositions of Pfister et al. and Powell et al. comprises cross-linked silicone, so they have inherent cross-link density. The compositions comprise a hydrophilic component. The compositions are topical patches, so they have inherent thickness. The compositions have an occlusivity to air, which may be zero or greater than zero. In any case, the active agents of Pfister et al. and Powell et al. are released at some rate, and the compositions inherently possess the physical properties of claims 62-65.

The selection of cross-link density, thickness of the composition, and occlusivity to air would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that the density of crosslinking is easily varied (Powell et al., Example 3), that the thickness of the composition would be varied depending on the size of the active agent and desired rate of release, and that the occlusivity to air varies with thickness and degree of cross-linking. A holding of obviousness over the cited claims is therefore clearly required.

The selection of hydrophilic component would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Powell et al. teach that the hydrophilic component may be polypropylene glycol (column 15, line 67). A holding of obviousness over the cited claims is therefore clearly required.

The selection of active agent would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Pfister et al. teach

that numerous diverse drugs are compatible with the topical preparation (column 8, lines 15-27). Powell et al. specifically contemplate an embodiment in which subtilisin, a protease, is the active agent (column 16, line 64, through column 17, line 5). The selection of enzyme would also have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that the enzyme may be selected depending on the desired activity of the composition. A holding of obviousness over the cited claims is therefore clearly required.

A person of ordinary skill in the art would have had a reasonable expectation of success in modifying the compositions of Pfister et al. or Powell et al. as discussed above because both compositions are taught as being optimizable for desired downstream applications. The skilled artisan would have been motivated to vary the degree of cross-linking, thickness of the composition, occlusivity to air, hydrophilic component, and active agent depending on the condition to be treated.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the compositions of Pfister et al. or Powell et al. as above because the prior art itself suggests such modifications.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 56-65 and 68-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 11, 12, and 14-16 of copending, currently commonly owned Application No. 10/385,213, which shares inventors with the instant application. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '213 application are drawn to a composition identical in scope with the composition employed in the instantly claimed method.

Claim 1 of the '213 application is drawn to a topical preparation comprising an internal phase and an external phase, wherein said internal phase is dispersed within said external phase; said internal phase comprises at least one hydrophilic carrier and at least one active agent; and said external phase comprises a silicone matrix. Instant claim 56 is drawn to a method of providing an active agent topically, comprising placing a topical preparation comprising an internal phase and an external phase, wherein said internal phase is dispersed within said external phase; said internal phase comprises at

least one hydrophilic carrier and at least one active agent; and said external phase comprises a silicone matrix in contact with a patient's skin. Instant claim 68 corresponds to claims 11 and 12 of the '213 application. Instant claims 69-71 correspond to claims 15 and 16 of the '213 application. As discussed above, instant claims 57-65 do not necessarily limit the physical or structural properties of the composition, so the scope of claim 1 of the '213 application encompasses the scope of each of these claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No claims are allowed.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Friday, 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SANDRA E. SAUCIER
PRIMARY EXAMINER

Lora E Barnhart

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